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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,146	02/11/2002	Stephen M. Testa	GERC 117991	7913

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EXAMINER	
RILEY, JEZIA	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,146	TESTA ET AL.	
	Examiner	Art Unit	
	Jezia Riley	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 4-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 4-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Remarks

1. Applicants' arguments, filed on 11.29.2004, have been approved and entered. They have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

Claim Objections

2. Claims 4, 6, 11, 13, 17, and 19 are objected to because of the following informalities: SEQ IDo:s, should not be in brackets. Brackets are used in amendments to show deletion of certain part of the claims. Therefore it is suggested that the SEQ IDNo:s not be in brackets to avoid confusion and deletion. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 14, 20 are indefinite at the recitation of "**capable of binding**" because

it cannot be determined whether the oligonucleotide do bind, because having the capability is not the same thing as actually performing the function. A positive recitation is required.

Claims 8-19 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 8 is indefinite because the claims do not recite **a final process step that clearly relates back to the preamble**. The claims are drawn a method of inhibiting self splicing of a Group I intron, however, the claim only recited a single step of "contacting a precursor RNA containing a Group I intron with an oligonucleotide.....". Thus it cannot be determined if the goal of the preamble, i.e., of inhibiting self splicing of a Group I intron is achieved or not and if achieved, in what step it is achieved. Same problem for claim 14 which is drawn to a method for inhibiting the growth of a organism comprising contacting said organism with an amount of an oligonucleotide effective for growth inhibition, but no step is specifically disclosed that clearly achieved the method and it is further unclear of what exactly is an effective amount. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion (see *ex parte Erlich*, 3 UsPQ2d1011, p.1011 (Bd. Pat, Applicant. Int.1986). Clarification is required as to Applicant's intent.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claim 8, 9, 14, 15, 20, 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Sullenger et al. (US5,869,254).

Sullenger et al. discloses Method for splicing a target nucleic acid molecule with a separate nucleic acid molecule. Splicing of the separate nucleic acid molecule with such a target nucleic molecule is designed to alter the protein product of that nucleic acid molecule. Such alteration causes production of a useful protein which will allow that cell to either survive or die, as desired. Thus, for example, in a gene therapy setting, the target nucleic acid molecule may encode a non-functional protein necessary for normal life. This molecule can be spliced with a separate nucleic acid molecule to allow appropriate expression of a functional protein. Alternatively, the splicing may cause production of a more stable protein, or of a protein which acts as an agonist or antagonist of a function, e.g., a viral or bacterial replication function. The target nucleic acid molecule can be any desired molecule with which a splicing reaction can occur which is viewed of the instant oligonucleotide comprising a chose sequence as claimed in instant claim20. Generally, this will be an RNA molecule, preferably a messenger RNA molecule which inherently comprises a 3'terminal ribonucleoside. The separate nucleic acid molecule is generally chosen such that it encodes a 3' exon which it is

desirable to express within a cell. By "enzymatic" or "catalytic nucleic acid molecule" is meant a molecule having a motif preferably selected from the motif of a group I or group II intron having a cleavage and splicing activity. By at least a portion of the respective nucleic acid molecules is meant that the 5' end of the target nucleic acid molecule will be spliced with the 3' end of the separate nucleic acid molecule. The method features catalytic nucleic acid molecules having a selected separate nucleic acid molecule as a 3' exon encoding at least a portion of a useful gene which can be used in gene therapy. Such a molecule can be spliced with and thereby correct or modify the expression of other target RNA molecules. (Summary of the invention, Figure 1, and examples).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 8-10, 14-16, 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sullenger et al. (US5,869,254) in view of Gryaznov (JACS, Vol.116, pp. 3143-3144, 1994).

Sullenger et al. discloses Method for splicing a target nucleic acid molecule with a separate nucleic acid molecule. Splicing of the separate nucleic acid molecule with such a target nucleic molecule is designed to alter the protein product of that nucleic acid molecule. Such alteration causes production of a useful protein which will allow that cell to either survive or die, as desired. Thus, for example, in a gene therapy setting, the target nucleic acid molecule may encode a non-functional protein necessary for normal life. This molecule can be spliced with a separate nucleic acid molecule to allow appropriate expression of a functional protein. Alternatively, the splicing may cause production of a more stable protein, or of a protein which acts as an agonist or antagonist of a function, e.g., a viral or bacterial replication function. The target nucleic acid molecule can be any desired molecule with which a splicing reaction can occur. Generally, this will be an RNA molecule, preferably a messenger RNA molecule witch inherently comprises a 3'terminal ribonucleoside. The separate nucleic acid molecule is generally chosen such that it encodes a 3' exon which it is desirable to express within a cell. By "enzymatic" or "catalytic nucleic acid molecule" is meant a molecule having a motif is preferably selected from the motif of a group I or group II intron having a

cleavage and splicing activity. By at least a portion of the respective nucleic acid molecules is meant that the 5' end of the target nucleic acid molecule will be spliced with the 3' end of the separate nucleic acid molecule. The method features catalytic nucleic acid molecules having a selected separate nucleic acid molecule as a 3' exon encoding at least a portion of a useful gene which can be used in gene therapy. Such a molecule can be spliced with and thereby correct or modify the expression of other target RNA molecules. (Summary of the invention, Figure 1, and examples). Sullenger does not show phosphoramidate linkages.

Gryaznov et al. teach oligonucleotide comprising phosphoramidate linkages are more stable that their natural phosphodiester compounds.

Therefore it would have been obvious at the time the invention was made to use an oligonucleotide containing at least one phosphoramidate linkage for the method of Sullenger. The motivation is that said oligos are more stable against degradation and bind more tightly with the RNA strand (Gryaznov page 3143, col.2). Chemical modifications of the phosphate backbone will reduce the negative charge thereby facilitating diffusion across the membrane. This principle has been successfully demonstrated for antisense DNA technology. (col. 14, lines 7-10). Establishment of therapeutic levels of ribozyme within the cell is dependent upon the rate of uptake and degradation. Decreasing the degree of degradation will prolong the intracellular half-life of the ribozyme. Thus, chemically modified ribozymes, e.g., with modification of the phosphate backbone, or capping of the 5' and 3' ends of the ribozyme with nucleotide analogs may require different dosaging.(col. 16, lines 4-12).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Wednesday, January 26, 2005

JEZIA RILEY
PRIMARY EXAMINER